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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,972	02/14/2002	Richard J. Whitley	UAB-16102/22	5479

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PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,972	WHITLEY ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2003 and 25 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-10 and 12-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10,12-18,22 and 23* is/are rejected.

7)☒ Claim(s) *19-21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 August 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20030925*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendments filed 8/29/03 and 9/25/03 have been entered. Claims 4 and 11 have been cancelled. Claims 1, 9 and 12 have been amended. Claims 16-23 have been added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

> The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive. The quote taken from MPEP 2164.02 relates to the sufficiency of the disclosure of a single working example and guidance concerning a genus as a whole to teach one of skill in the art how to use a generic invention. However, the issue here is the sufficiency of the written description of the provisional applications to show that Applicant was in possession of the instantly claimed invention and to place the instantly claimed invention into the hands of the public. Consequently, MPEP 2164.02 is not applicable. The provisional applications teach single species of replication competent HSV-1 vectors, where both copies of the γ34.5 gene are replaced with transcription cassette consisting of an Egr-1 promoter and polyA sequence

operably linked to coding sequences for IL-12 or GM-CSF (60/138,173) or *E.coli* cytosine deaminase (60/144,314), and no other genetic alterations to the HSV-1 genome. Claim 1 of each only stipulates that a HSV vector comprise coding sequence for one of these three proteins, with no limitations on whether the HSV vector is replication competent, deficient or restricted; the placement of the transgene, the promoter or other elements linked to the transgene, or any other details of the generic vector. The instant claims lie between these two extremes, and there is no support for this genus in the provisional applications.

Drawings

The drawings were received on 8/29/03. These drawings are not acceptable. New corrected drawings are required in this application because no detail can be discerned in Figure 2. Where the original Figure 2 showed a picture of black bands on a white background, new Figure 2 shows only a blackened rectangle. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 16 and 23 are directed to embodiments were the promoter is a mammalian promoter. Applicant has not indicated where this new limitation is supported by the original disclosure, as is their burden to do. MPEP 714.02, last sentence of the third paragraph from the end and 2163.06 (I) last sentence. The original specification (page 9) teaches either inserting the nucleic acid sequence encoding the agent into the HSV genome so as to be under control of a viral promoter or to insert it operably linked to the murine Egr-1 promoter. While the Egr-1 promoter is a mammalian promoter, there is no indication that linking the nucleic acid to other mammalian promoters or to a generic mammalian promoter was contemplated by Applicant. Thus, there is no evidence that Applicant was in possession of this genus when the original invention was made.

Claim Rejections - 35 USC § 102

Claims 1-3, 5, 9, 10, and 13-15 remain rejected under 35 U.S.C. 102(e) as being clearly anticipated by Wechsler et al. US 2002/0098170 for the reasons of record set forth in the Office action of 4/3/03.

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive. All of Applicants arguments rely upon a declaration made by Richard J. Whitely

under 37 CFR 1.131. However, the Whitley Declaration filed on 8/29/03 under 37 CFR 1.131 is improper and has not been considered. A declaration 37 CFR 1.131 must be made by all inventors of the claimed subject matter to which the declaration pertains. MPEP 715.04. No evidence has been presented that Whitley is the sole inventor of the claimed invention to which the rejection and declaration applies.

Claims 17, 18, and 22 are rejected under 35 U.S.C. 102(a), (b) & (e) as being clearly anticipated by DeLuca, US 5,804,413, for the reasons of record as applied to claims 9, 10 and 15 in the Office action of 4/3/03.

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive. With respect to rejection under §102(b), as indicated above, the broad claims do not enjoy benefit of priority to either provisional application. Furthermore, the subject matter disclosed by DeLuca is not described in either provisional application. The disclosure of the '314 provisional application is limited to a single species that is not taught in DeLuca. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., replication competent HSV) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Limiting claim 17 to replication competent HSV vectors would overcome this rejection.

Claims 1, 2, 9, and 15 remain rejected and claim 16 is rejected under 35 U.S.C. 102(e) as being clearly anticipated by Boursnell et al., US 6,287,557 for the reasons of record set forth in the Office action of 4/3/03, and the additional reason set forth below.

New claim 16 recites that the promoter is a mammalian promoter. Boursnell teaches that the promoter operably linked to the heterologous nucleotide sequence, such as encoding GM-CSF, can be a mammalian promoter (col. 9, lines 40-59).

Claims 1, 2, 9, and 15 remain rejected and claim 16 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Inglis et al., WO 96/26267 for the reasons of record set forth in the Office action of 4/3/03, and the additional reason set forth below.

New claim 16 recites that the promoter is a mammalian promoter. Inglis teaches that the promoter operably linked to the heterologous nucleotide sequence, such as encoding GM-CSF, can be a mammalian promoter (page 13, lines 2-19).

Claims 1, 2, 9, and 15 remain rejected under 35 U.S.C. 102(a) as being clearly anticipated by Todryk et al. (Hum. Gene Ther. 10 (17): 2757-2768, 20 Nov. 1999) for the reasons of record set forth in the Office action of 4/3/03.

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive. In response to applicant's argument that the Boursnell, Inglis and Todryk references fail to show certain features of applicant's invention, it is noted that the feature upon which applicant relies (i.e., the vector produces infectious particles) is not recited in the rejected

claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). With respect to Todryk, the instant application does not enjoy benefit of priority to the provisional applications for the generic invention being claimed. The HSV-1 vectors taught in the provisional applications are not the same as taught in Todryk.

Claim Rejections - 35 USC § 103

Claims 9, 12 and 13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wechsler et al. US 2002/0098170 in view of Toda et al. (J. Immunol. 160 (9): 4457-4464, 1 May 1998) for the reasons of record set forth in the Office action of 4/3/03.

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive. All of Applicants arguments rely upon a declaration made by Richard J. Whitely under 37 CFR 1.131. However, the Whitley Declaration filed on 8/29/03 under 37 CFR 1.131 is improper and has not been considered. A declaration 37 CFR 1.131 must be made by all inventors of the claimed subject matter to which the declaration pertains. MPEP 715.04. No evidence has been presented that Whitley is the sole inventor of the claimed invention to which the rejection and declaration applies.

Claims 1-3, 5-10, 12-15 remain rejected and claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andreansky et al. (Gene Therapy 5 (1): 121-130, Jan. 1998) in view of Toda et al. (J. Immunol. 160 (9): 4457-4464, 1 May 1998) for the reasons of record set forth in the Office action of 4/3/03.

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive. First, Applicant argues that since inclusion of IL-4 had different effects than inclusion of IL-10, that one of skill in the art would not have a reasonable expectation of success in substituting other cytokines. However, it is respectfully submitted that Andreansky was initially determining whether the oncolytic effect of replication competent HSV was mediated solely by the HSV replication or whether the immune system played a role. If the latter, then inclusion of a transgene encoding IL-4, known to inhibit tumor growth by stimulating localized inflammatory or immune response, was expected to increase the cytolytic effect, while inclusion of IL-10, an immunosuppressive cytokine, would be expected to blunt the cytolytic effect (see page 121, col. 2 to page 122, col. 1). Andreansky showed that indeed the oncolytic effect of replication competent HSV was mediated in part by immune response, and that expression of cytokines known to inhibit tumor growth increased the potency of the HSV.

Second, Applicant argues that Toda teaches away from incorporating the IL-12 gene into the replication competent HSV, since in the last paragraph of the Discussion, Toda speculates that the presence of multiple copies of the IL-12 gene in particles separate from the replication competent HSV "may account for the significant anti-tumor effect." However, It is respectfully submitted that Applicant has taken this paragraph out of context. The goal of Toda was to determine if local expression of IL-12 would act as an adjuvant for oncolytic infection with attenuated replication competent HSV. Toda does not address the issue of whether the same effect would or would not be expected had the IL-12 gene been incorporated into the replication competent HSV.

Furthermore, the issue is not whether it would have been obvious to replace the two HSV system of Toda with the single HSV system of Andreansky, but whether it would have been obvious to have incorporated an IL-12 gene into the vector of Andreansky, since Andreansky teaches genes for a variety of cytokines known to inhibit tumor growth could be used, including GM-CSF (page 122, col. 1). Toda teaches that expression of IL-12 was superior to GM-CSF (page 4462, bottom of col. 2). Andreansky omitted IL-12 from the list, and Toda clearly demonstrates why IL-12 would have been an obvious alternative to the cytokines listed by Andreansky, such as GM-CSF.

Allowable Subject Matter

Claim 19, 20 and 21 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

DeLuca does not disclose including a cytosine deaminase gene into a replication competent HSV, nor does it disclose deleting a γ34.5 gene. Chiocca teaches replication competent (or restricted) HSV vectors comprising a suicide gene. However, Chiocca explicitly teaches away from making such vectors where the suicide genes encode HSV-TK or *E. coli* cytosine deaminase (col. 17, lines 50-65), because the toxic nucleotides produced by the action of these enzymes upon their respective prodrugs would be expected to impair replication of the HSV, and thus the cytotoxicity of the replication competent HSV – defeating the purpose of using a replication competent HSV vector versus a replication deficient vector, such as used by DeLuca.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe
Primary Examiner
Art Unit 1632

Scott D. Priebe